REMARKS

Claims 57-61 are active in this application.

The presently claimed invention is drawn to a method for suppressing bacterial growth in a blood fraction, comprising adding to a blood fraction a compound selected from the group consisting of L-carnitine, salts of L-carnitine, alkanoyl carnitines, salts of alkanoyl carnitines, and mixtures thereof, in an amount effective to suppress bacterial growth in said blood fraction,

wherein said blood fraction is a *prestorage-leuko-reduced* platelet concentrate, and wherein said method comprises suspending said *prestorage-leuko-reduced* platelet concentrate in a support solution which comprises said compound. (see Claim 57) Applicants submit that the combined disclosures of Sweeney et al, US 5,747,536, Tegos et al, and Ogawa et al can not affect the patentability of the claimed invention and reconsideration of the outstanding rejections is requested in view of the amendments and remarks herein.

The rejection of Claims 57-61 under 35 U.S.C. §103(a) over Sweeney et al in combination with US 5,747,536, Tegos et al, and Ogawa et al is respectfully traversed.

In the Advisory Action mailed November 6, 2008, the Examiner indicates that she has maintained the rejection over Sweeney et al in combination with US 5,747,536, Tegos et al, and Ogawa et al. Although the Examiner acknowledges that Sweeny et al does not disclose leukodepleted platelet concentrates or that there is a problem with bacterial growth in platelets, the Examiner alleges that the claimed invention is a "discovery of a different biological mechanism than was previously understood behind the administration of a known bioactive compound". Thus, the Examiner concludes that the subject matter of the present

application is "clearly publishable in a peer-review journal" but does not meet the "criteria for patenting claims". Specifically, the Examiner continues to allege that the claimed invention is obvious because "it is the same one step method of administering the same compound to an *obvious variant* of a platelet composition."

Applicants continue to disagree and contend that the Examiner has not properly examined the present application. Indeed, Applicants submit that the Examiner has failed to demonstrate how the claimed invention is a nothing more than a "discovery of a different biological mechanism than was previously understood behind the administration of a known bioactive compound". As stated above, the claimed invention relates to "a method for suppressing bacterial growth in a blood fraction, comprising adding to a blood fraction a compound selected from the group consisting of L-carnitine, salts of L-carnitine, alkanoyl carnitines, salts of alkanoyl carnitines, and mixtures thereof, in an amount effective to suppress bacterial growth in said blood fraction" (see Claim 57). This is not a discovery of a different biological mechanism, but rather represents new way to suppress bacterial growth in clinically important biological samples (i.e., a blood fraction). Prior to the present invention, for the reasons detailed below as restated from the response filed on September 15, 2008, the artisan was not in possession of this invention and, thus, the claimed invention is novel and non-obvious.

Specifically, Applicants submit that Sweeney et al do not disclose or suggest the treatment of a prestorage-leuko-reduced platelet concentrate. On the contrary, Sweeney et al use standard non-leuko-reduced platelet concentrate (see page 31, line 13). Thus, the material used in the presently claimed invention differs from that disclosed in Sweeney et al.

At the outset, Applicants wish to establish the correct background of the present invention in the light of the knowledge of the skilled artisan at the time of the present

invention. Against this background Applicants submit that the claimed invention is not obvious.

First, the skilled artisan would be expected to be competent in the art of blood and blood product storage. As depicted in the specification of the application (see Discussion of the Background), stability upon storage is the main problem for blood and blood product supplies (page 2). In this regard, Applicants report what is known in the general knowledge of the art at the time of the present invention. Specifically, Applicants explain that viability and/or short circulation life upon infusion are due to glycolysis (page 2, lines 14-17).

Applicants further explain that contamination of blood supplies by bacteria is presented as a separate problem (page 2, line 19, page 3, lines 21-22 – "*is another problem to be addressed*"). This problem is still perceived as *separate* from the problem of extending viability (page 20, lines 19-21 and following; page 7, line 21 – "*The inventor has also discovered*"). Clearly, as set forth in the specification, suppressing bacterial growth and reducing glycolysis are *two separate* problems (page 7, line 24 – "*The inventor has further discovered*") and conducted *two* different experiments to demonstrate the advantages of the claimed invention, one for each problem(page 30, experiment I and page 31, experiment II).

Sweeney et al, which is cited by the Applicants in the specification (page 30 and 31) and discussed in the previous responses, teach reduction of glycolysis by L-carnitine and acetyl L-carnitine in non-leuko-reduced platelet concentrates. Sweeney et al suggest that addition of L-carnitine or acetyl L-carnitine may improve platelet concentrate *quality*. Not once do Sweeney et al disclose or suggest that there even exists a problem of *contamination*. In the context of the general knowledge in the art at that time of the present invention, the problem of contamination is solved through irradiation of blood and blood products, which, on the other hand, affects quality (specification, page 28, line 7-20).

Ogawa et al deals with the problem of adverse effects brought about by white blood cells (WBC) contaminating platelet concentrates (first page, right column). It should be noted that the only other contamination cited by Ogawa et al is viral contamination (ibid.), but no solutions are devised. The skilled artisan will recognize that WBC contamination is a different problem than bacterial contamination. These problems are also differently treated in the present application (see page 27, line 13 and following for TA-GVHD).

Neither Sweeney et al nor Ogawa et al disclose or suggest the problem of bacterial contamination, nor is there any relation between these two references. Ogawa et al do not disclose glycolysis in relation to WBC contamination, hence leuko-reduction.

The present invention is not drawn to a method for leuko-reduction (see page 30-31 where commercially available filters are used for this purpose), but rather is drawn to a method for suppressing bacterial growth. It is herein stressed out that reducing glycolysis, either in non leuko-reduced or in leuko-reduced PCs, is different from suppressing bacterial growth. None of the cited references, either alone or in combination, deal with this problem.

Whenever true that reducing glycolysis according to Sweeney et al would have implicitly suppressed bacterial growth, the skilled person would have recognized this result and would not have resorted to irradiation, thus continuing to face the problem of quality affected by irradiation (see specification). However, this was not the case. As a result, prior to the present invention, the skilled artisan continued to irradiate blood products to suppress bacterial growth.

US 5,747,536 discloses the equivalence of the various acyl carnitines, but in a completely different context. The use of said compounds in the treatment of cardiovascular, disorders, peripheral vascular diseases and peripheral diabetic neuropathy cannot be taken into consideration by the person of ordinary skill in the art of *platelet storage*. This skilled

artisan would be totally unaware of method of treatment of cardiovascular, disorders, peripheral vascular diseases and peripheral diabetic neuropathy and would not address his attention there to try to find a possible suggestion with respect to platelet storage. Thus, US 5,747,536 fails to offer anything further to the disclosure of Sweeney et al.

Tegos et al is disclose "*Depletion of glycolytic enzymes does not seem to be a major factor in the storage lesion of platelets*". As in the presently claimed invention, Tegos et al study platelet concentrates free from contaminating leukocytes (i.e. leuko-depleted platelet concentrates). Therefore, the skilled artisan, in the view of Tegos et al, would not continue with the method disclosed by Sweeney et al or even to combine these two disclosures,

Again, neither Sweeney et al nor Tegos et al disclose inhibition of bacterial growth in platelet concentrates and the art gives no relationship between reducing glycolysis in a platelet concentrate and inhibiting bacterial growth in the same concentrate. Thus, it would not be apparent that glycolysis could be related with bacterial growth. Therefore, the present invention relates to a previously unappreciated and unpracticed invention.

The Examiner states that Applicants did not point to the exemplification of the better results achieved by the present invention. It is respectfully indicated on top of page 31 of the specification there is the demonstration that platelet concentrates were safely stored for 8 days. With respect to 3 days of the state of the art (see Ogawa and Tegos in this respect), this is a dramatic enhancement in storage of blood product.

Applicants respectfully submit that the skilled artisan assigned with the task of finding a method for inhibiting microbial growth in a platelet concentrate would not find any direction toward the presently claimed invention in the cited combination of references.

An expectation of success must be indicated in the art. If not, the skilled artisan is left alone with information which cannot be used consciously. In the present case, the artisan is

not lead to the problem, let alone to the inventive solution. Indeed, the cited references fail to provide any disclosure or suggestion of problems with inhibiting bacterial growth. In fact, the general knowledge solves the problem by irradiating, which would be detrimental to quality.

The cited references fail to disclose or suggest that reducing glycolysis would inhibit bacterial growth. In fact, the cited references never pushed platelet concentrate storage over 72 hours (Tegos et al and Ogawa et al). Sweeney et al made a step forward reaching 5 days, but only in view of reduction of glycolysis (however, Tegos et al conclusions must be taken into account). Nevertheless, the skilled artisan, even in view of Sweeney et al results, would have still resorted to irradiation for facing the problem of microbial contamination.

Moreover, the present invention achieves an improved result in that storage time is extended to 8 days (specification, page 31). In this art, progress is made by little steps, but every extension of storage life is of utmost importance in saving lives of human beings. For example, in disaster situations (e.g., a hurricane, an earthquake, a terrorist attack) availability of blood supply is critical and every single day of extended storage is critical. Despite this critical need, no one in the art reached 8 day storage before the present invention.

In the outstanding Office Action, the Examiner asserts that the demonstration in the Example on pages 30-31 of the specification that the claimed invention provides storage of platelets of 8 days is irrelevant. The basis for this position is, in part, that 8 days of platelet storages is not a claim limitation. Applicants are not aware of any legal authority that has held that the evidence shown to rebut a *prima facie* case of obviousness is only probative when the result of that data (i.e., the magnitude of the benefit) is specifically claimed. Indeed, if this were the case, how could "commercial success" be a secondary consideration to establish non-obviousness? Certainly, it could not.

The Examiner is reminded that "Evidence of unobvious or unexpected advantageous

properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987)" (see MPEP §716.02(a)). The *Chupp* decision can and should be applied to methods, as well. Where Applicants can demonstrate that a claimed method provides an unexpected result as compared to the cited art, such a result (regardless of whether claimed or not) should be considered.

Thus, for the reasons given above and based ion the advantages clearly shown in the present specification, Applicants submit that the present invention is not obvious over the combined disclosures of Sweeney et al, US 5,747,536, Tegos et al, and Ogawa et al. Specifically, Applicants submit that absent the present application the skilled artisan would not have known or assumed that by adding acetyl L-carnitine to platelet concentrates, even if by the same method as Sweeney et al to reduce glycolysis, would have attained the result to suppress bacterial growth and prolong storage time of the concentrates.

In view of the foregoing, withdrawal of these grounds of rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Vincent K. Shier, Ph.D.
Registration No. 50,552

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)